REMARKS/ARGUMENTS

Claims 1 and 3 are active in this case. Claim 1 has been amended to incorporate the limitations of Claim 2, which has been cancelled. Support for new Claim 3 is found on pages 4 and 11.

The specification is amended to remove the typographical error noted on page 2 of the Official Action and also to correct the phrase "antibody value" to be "antibody titer."

No new matter is added by these amendments.

Applicants thank Examiner Kapushoc and Examiner Switzer for the courtesy of discussing this case with their undersigned representative on January 30, 2006. During this discussion, the undersigned explained that as described in the specification, e.g., on page 21 last paragraph, the claimed method for examining the caries risk finds unique applicability in that one can examine caries risk irrespective of the age and the salivary quantity as compared with a conventional immunity method by assessing the correlation between antibody titers directed to a specific peptide (SEQ ID NO:1) and using this antibody titer correlation to assess the risk of caries in an individual based on a DRB*1 HLA class II genotype. This method provides are more accurate testing method thereby having great value in the field of dental medicine. Moreover, this method has particular advantages for assessing caries risk in infants, less than about 6 years of age, due to their incomplete immune system and for which traditional immunological methods would not sufficiently detect the caries risk (see page 5, last paragraph of the specification).

In addition, it was agreed that upon incorporation of Claim 2 into Claim 1, the rejections raised under 35 USC 102(b) would be withdrawn (see Interview Summary). As noted above, Claim 1 has been amended in this manner and therefore it is requested that the rejections under 35 USC 102(b) in view of Ozawa et al. and Acton et al. be withdrawn.

During this meeting the obviousness rejection in view of Acton et al., Matsushita et al., and Senpuku et al was also discussed. In particular, the undersigned explained that these publications do not disclose or suggest the claimed method for evaluating a relative risk for developing dental caries by determining a reference standard that may be used for comparing measured levels of anti-PAc antibodies and HLA-DRB genotype of subjects against the reference standard.

Acton et al. describes a correlation between HLA-DRB1 genotype and *S. mutans* levels evaluated in representative subjects. In Acton, there is simply a correlation between levels of bacteria and genes; no relationship of assessed DRB genotypes to caries risk is described.

Matsushita et al. describes multiple antigenic epitopes identified within the full-length of PAc (FIGS. 3-5) by reacting synthetic peptides of PAc with serum and saliva samples removed from some subjects. In the last paragraph of the discussion (page 4040, second column), Matsushita simply suggest the potential for using the epitopes for developing a diagnositic test or a vaccine. Nothing in this publication provides any indication that one could correlate DRB1 genotypes with caries risk.

The basis of the rejection is outlined in the Office Action, in that it has been alleged that it would have been obvious to modify the method of Acton et al., to include the antibody-based method of Matsushita et al. to determine the caries risk of an individual (last line of page 14 of the Official Communication). However, as is readily apparent from the actual disclosures of these references, even if Acton were modified with Matsushita, one would not be in possession of the claimed method because neither of these two publications correlate DRB1 genotypes to caries risk.

It is also alleged that it would have been obvious to use synthetic peptides of PAc (361-386) by combining the peptides PAc (355-373) and PAc(369-387) taught by Senpuku et al. that suggest the use of the antigenic properties of both peptides in the claimed method (last sentence of page 15 of the Official Communication). However, Senpuku et al. describes several HLA-DR-binding motifs/regions identified in PAc. As discussed throughout the article and, for example in the Abstract, these peptides were identified and were believed to be relevant for providing a therapy for treating dental caries. Nothing in this article would lead one to understand a correlation between DRB1 genotypes and caries risk. Therefore, unlike the claimed invention, the combination of these three articles provides no direction that would render the claimed method obvious.

It should also be noted that during the above-noted meeting between the Examiner's and the undersigned, it was also proposed to restrict the particular antigenic peptide used for establishing a relationship between DRB1 and dental caries risk to the peptide "consisting of SEQ ID NO:1." Although not specifically referred to in the Interview Summary form of January 30, 2006, it is understood that this limitation also provides a point of difference between the claims and the articles cited in the 103 rejection. Specifically, since there is nothing in any of the three articles which would lead one to the specific SEQ ID NO:1 amino acid sequence (and in particular nothing in Senpuku), the claimed invention could not have been obvious in view of the combination of citations.

On the basis of the above-discussion, it is requested that the rejection under 35 USC 103 be withdrawn.

To the rejection under 35 USC 112, first paragraph, in which it has been alleged that the specification does not provide sufficient guidance to enable the claimed method for predicting the risk for developing dental caries based on one exemplary study in which only five individuals having different genotypes were evaluated for sIgA titers. During the above-noted meeting between the Examiners and the undersigned, this rejection was discussed as well, they reiterated that, it is their position, that to enable the claimed method, a statistically significant number of individuals in a controlled study must be evaluated in order to establish reference values for comparing sIgA levels and HLA-DRB1 genotype that can be measured in evaluated subjects. Moreover, they expressed concern that the alignment in Table 1 of the specification do not show correlation between genotypes in general and caries risk. They, therefore, requested additional evidence as to the applicability of comparing DRB1 genotypes and caries risk. To that end, attached is such evidence in the form of a Declaration under 37 CFR 1.132 (executed).

As discussed in the Declaration, one can correlate the relationship between antibody titer and genotype that is prior to the claimed method. As discussed in the specification, using this type of correlation, one can simply obtain a sample from a subject identify the DRB*1 genotype, compare it to the correlation to assess whether the subject is at risk of developing caries based on the genotypes identified from the subject. In other words, if the subject has a genotype that has been correlated to the high group, then that subject is at risk of developing dental caries.

Accordingly, withdrawal of this ground of rejection is requested.

The rejection of Claims 1 and 2 under 35 USC 112, second paragraph is believed to be addressed by the amendments.

Claim 1 has been amended to incorporate Claim 2 and therefore any criticisms of original Claim 1 should no longer be applicable as the steps used for determining caries risk have been set forth in the body of Claim 1.

As for how to identify a genotype, it should now be clear that the genotype is identified from a subject and obtaining a genetic sample and determining its sequence or otherwise is well within the skill in this field, e.g. using PCR (see also the specification on pages 13-17).

As to what is meant by "identified beforehand," it should now be clear that the genotypes correlating to caries risk is determined prior to carrying out the claimed method and the correlation between genotype and caries risk is drawn from the relationship of genotypes and antibody titers that in themselves correlate to high and low caries risk. For further guidance on this point see the discussion on pages 20-21 of the specification culminating in Table 1 on page 20.

Withdrawal of this ground of rejection is requested.

Applicants also request a Notice of Allowance indicating that Claims 1 and 2 have been allowed.

Respectfully submitted,

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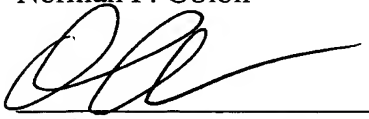

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